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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,406	OKABE ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,14-16,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,14-16,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/10/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The notice of allowance sent on 04/16/2009 is withdrawn according to the petition decision of 04/20/2009 to allow reopening of the prosecution because inadvertent misunderstandings regarding the claim language talked about between the examiner and Applicant's representative Kevin Bastian on 04/03/2009. Consequently the list of pending claims that is considered is the one submitted on 01/16/2009 with the response to the non-final rejection. Claims 1, 2, 4-6, 14-16 are amended and claims 3, 7-13 and 17-21 have been canceled. New claims 22 and 23 have been added. Claims 1, 2, 4-6, 14-16, 22 and 23 are pending and are currently examined.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 01/19/2004. It is noted, however, that applicant has not filed a certified copy of the 2004-010971 application as required by 35 U.S.C. 119(b).

Maintained and new claim rejections necessitated by amendment

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 4-6, 14-16, 22 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The independent claims 1, 2, 14-16, 22 and 23 are indefinite because they contain the limitation "derivative thereof". This limitation is not adequately described (see below) and as such the metes and bounds of the claims could not be determined. Claims 4-6 are rejected as dependent claims.

5. Claims 16 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the dosage or the time frame of starting or stopping of the treatment. Without these steps, a person of ordinary skill in the art would not know when to start the treatment and when the treatment has achieved its goal and what dosage is necessary for attaining the goal of the treatment. As such, the metes and bound of the claims could not be determined.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 4-6, and 14-16 remain and claims 22-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the

time the application was filed, had possession of the claimed invention for the reasons of record. As specifically iterated in the previous office action, the only adequate written description in the specification is offered for the antibody #33 for which the sequences of the variable heavy and light chains as well as the sequences of all CDRs are presented (p. 9 line 9 to p. 10 line 14). There is no description of a derivative of the antibody and no guidance in the specification as what this recitation actually encompasses. There is also no description of the mutation(s) envisioned and the specific locus that they are made. The description of one antibody (Ab #33) is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all derivatives thereof.

On page 8 of the Remarks Applicant argues that due to the amendments to the claims they have adequate written description. The arguments were carefully considered but not found persuasive because as explained in the previous office action only the exact sequences specifically describe the antibody of the invention. Any alterations (mutations, insertions or deletions), in absence of the description of the exact position would not fulfill the requirements for description of a functional component of the genus claimed. Also, there is still no description of the derivatives intended to be encompassed by the claims.

8. Claims 1, 2, 4-6, and 14-16 remain and the claims 22-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antibody having the heavy chain variable region comprising SEQ ID NO: 4 and the light chain variable region comprising SEQ ID NO: 8 or having three CDRs from either the

heavy or light chain (SEQ ID NOs. 1-3 or 5-7, respectively), does not reasonably provide enablement for any other derivative thereof . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims for the reasons of record.

To summarize, the rejection relates to obtaining an antibody or has a number of undisclosed deletions, substitutions or additions within the heavy or light chain variable regions. As iterated in the prior Office action, an antibody is fully defined by at least three CDRs form the same variable region chain. If mutations are contemplated in the heavy chain or light chain than they have to be done in such a manner that the CDRs are not affected because that would destroy the binding properties of the particular antibody which may render the antibody non-functional. In order to be functional, such a molecule has to be an antibody which has necessary requirements (which are attained by Antibody #33 of the instant Application). Also, the recitation “derivative thereof" lacks adequate written description; one cannot make that which is not described.

Another issue regarding the use of antibodies of the invention is their use in the prevention of a disease. Claims 14-15 require a method of preventing an inflammatory disease or hypercytokinemia. However, the phrase "preventing a disease", given its broadest reasonable interpretation in light of the teachings in the specification, requires that absolutely no cell, nor tissue, or individual would present any symptom of a disease after treatment with antibody #33. There is no evidence, either in the specification or in the prior art, that any method to date can accomplish this goal. The specification

presents the results of experiments demonstrating that the use of the antibody may significantly inhibit the production of cytokines but not totally abolish it (Example 2). However, there is no support for the prevention of any disorder or disease, as is required by the claims, and neither can such support be obtained through reasonable extrapolation of the data or teachings in the art.

The working examples disclosed in the specification provide enablement only for the Ab#33 but not for other antibodies claimed and not for the prevention aspect of the method claimed. Therefore, it is considered that, because of the large quantity of experimentation necessary to generate the unknown number of potentially binding molecules recited in the claims and possibly screen the same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the absence of working examples directed to same; the state of the prior art which establishes the unpredictability regarding obtaining antibodies with desired properties based on less than the full complement of the six CDRs, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

9. On page 8 of the Remarks Applicant argues that due to the amendments to the claims they are now enabled. The arguments were carefully considered but not found persuasive because as explained in the previous office action only the antibody #33 (described by the exact sequences claimed) is enabled to make or use the invention. Any alterations (mutations, insertions or deletions, derivatives), in absence of the description of the exact position would not fulfill the requirements for description of a

functional component of the genus claimed and thus a person of ordinary skill in the art would not be able to make and use the invention without undue experimentation . Also, undue experimentation would be needed to ensure that the prevention aspect of the invention is actually occurring.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Plow et al. (U.S. Pat. No. 5,149,780).

Plow et al. teach antibodies that react to a polypeptide derived from the Arg-Gly-Asp (RGD) binding region of the Integrin beta subunit (GPIIIa- a synonym of the CD61 and their use to modulate Integrin-ligand binding. The region used for raising antibodies is between residues 110-170 of the sequence of the GPIIIa protein (abstract; col. 5, line 64 to col. 6, line 32). The region is in the extracellular domain as can be seen from the evidentiary reference from the web site entry http://www.uniprot.org/uniprot/P05106. The antibodies may be polyclonal or monoclonal col. 9, line 20 to col. 11, line 68). Compositions comprising the antibodies are taught and in vivo therapeutic uses for the antibodies encompass modulation of inflammatory responses (Col. 12, lines 1-66). Since Plow et al. taught the use of their antibodies for therapeutical modulation of

inflammatory processes, by performing the methods of Plow et al. a skilled artisan would necessarily perform the invention claimed in 16 and 22-23.

Thus the claims 16 and 22-23 are anticipated by Plow et al.

11. Claims 1-2 and 4-6 remain rejected under 35 U.S.C. 102(b) as being anticipated by Reiner et al. (J. Immunol. Meth., 184, 153-162, 1995-cited previously) for the reasons of record.

The claims are interpreted such that the limitation "derivative thereof", since it is not adequately described, in the broadest reasonable interpretation, would encompass the antibody of Reiner et al. Therefore, the antibody of Reiner et al. anticipates the claims 1-2 and 4-6

On page 9 of the Remarks Applicant argues that Reiner et al. do not teach the exact antibody (Antibody #33) of the instant Application. The arguments were carefully considered but not found persuasive because the claims interpretation, iterated supra, the antibody of Reiner et al. encompass a "derivative" of the antibody #33. As such, its properties would be dictated by its structure and not by intended use.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Plow et al. (U.S. Pat. No. 5,149,780) in view of Queen et al. (U.S. Pat. No. 5,693,762).

The claim is drawn to a pharmaceutical comprising chimeric or humanized anti-CD61 antibody for use in a method of treatment of an inflammatory disease based on hypersecretion of inflammatory cytokines.

The teachings of Plow et al were presented *supra*. Plow et al. are silent about the use of chimeric or humanized antibodies in their compositions or methods.

Queen et al. teach methods for producing, and compositions of, humanized immunoglobulins having complementarity determining regions (CDR's) and possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided. When combined into an intact antibody, the humanized immunoglobulins will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such as a protein or other compound containing an epitope (abstract). Humanized antibodies have at least three potential advantages over mouse or in some cases chimeric antibodies for use in human therapy:

1) Because the effector portion is human, it may interact better with the other parts of the human immune system (e.g., destroy the target cells more efficiently by complement-dependent cytotoxicity (CDC) or antibody-dependent cellular cytotoxicity (ADCC)).

2) The human immune system should not recognize the framework or constant region of the humanized antibody as foreign, and therefore the antibody response against such an injected antibody should be less than against a totally foreign mouse antibody or a partially foreign chimeric antibody.

3) Injected mouse antibodies have been reported to have a half-life in the human circulation much shorter than the half-life of normal antibodies. Injected humanized antibodies will have a half-life more similar to naturally occurring human antibodies, allowing smaller and less frequent doses to be given.

It would have been obvious for a person of ordinary skill in the art at the time that the invention was made to modify the antibodies of Plow et al. with the methods of Queen et al. and obtain antibodies better suited for therapy with a reasonable expectation of success because known and tested methods would be followed. The motivation to do so is expressed by Queen et al. which underscore the advantages of humanized antibodies for therapy.

16. Claims 16 and 22-23 rejected under 35 U.S.C. 103(a) as being unpatentable over Reiner et al. (J. Immunol. Meth., 184, 153-162, 1995-cited previously) in view of Plow et al. (U.S. Pat. No. 5,149,780).

The claims are drawn to a method of treatment of an inflammatory disease based on hypersecretion of inflammatory cytokines of an anti CD61 antibody or derivative thereof.

The teachings of Reiner et al. were presented *supra.* They do not use their antibody for treatment.

As presented above, Plow et al. teach antibodies that bind CD61 and their use to modulate Integrin-ligand binding.

The antibody of Reiner et al. would bind the CD 61 and thus could be used in the method and composition of Plow et al.

It would have been obvious for a person of ordinary skill in the art at the time that the invention was made to have tried and used the antibody of Reiner et al. in the methods and compositions of Plow et al. with a reasonable expectation of success because both antibody bind the same antigen. Plow et al. was trying to find a way to for

therapeutical modulation of inflammatory processes using anti –CD61 antibodies. The Supreme Court stated in KSR: When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product is not of innovation but of ordinary_ skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int'l Co. v. Teleflex Inc., 127 S. Cl. 1727, 82 USPQ2d1385, 1397 (2007).

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 9:00-18:30 M-Th and 9:00-18:30 alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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